

**Notice of Allowability**

Application No.

09/124,280

Examiner

N. M. Minnifield

Applicant(s)

PORRO, MASSIMO

Art Unit

1645

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--**

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 4/1/03; 4/4/05.
2. ☒ The allowed claim(s) is/are 1-8, 10-17, 19-35 and 37-64; now renumbered 1-61 respectively.
3. ☐ The drawings filed on \_\_\_\_\_ are accepted by the Examiner.
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some\* c) ☐ None of the:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\* Certified copies not received: \_\_\_\_\_.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

**THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.**

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
6. ☒ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
- (a) ☒ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
- 1) ☐ hereto or 2) ☒ to Paper No./Mail Date 10/8/99.
- (b) ☒ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date attached.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

**Attachment(s)**

1. ☒ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO-1449 or PTO/SB/08),  
Paper No./Mail Date \_\_\_\_\_
4. ☐ Examiner's Comment Regarding Requirement for Deposit  
of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☒ Interview Summary (PTO-413),  
Paper No./Mail Date attached.
7. ☒ Examiner's Amendment/Comment
8. ☐ Examiner's Statement of Reasons for Allowance
9. ☐ Other \_\_\_\_\_

## EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with James V. Costigan, 25669 on April 4, 2005.

All rejections have been withdrawn in view of the amendment to the claims and the comments/arguments set forth in the Appeal Brief.

The application has been amended as follows:

1. (currently amended) A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide, on a weight basis relative to said LPS, said peptide [comprising:] selected from the group consisting of:
  - (a)  $(A)_n$  wherein A is Lysine or Arginine and n is an integer with a minimum value of 7;
  - (b)  $(AB)_m$  wherein A is Lysine or Arginine and B is a hydrophobic amino acid selected from the group consisting of Valine, Leucine, Isoleucine, Tyrosine, Phenylalanine and Tryptophan; m is an integer with a minimum value of 3; and
  - (c)  $(ABC)_p$  wherein A is a cationic amino acid which is Lysine or Arginine; B and C are hydrophobic amino acids which may be the same or different and are selected from the group consisting of Valine, Leucine, Isoleucine, Tyrosine, Phenylalanine and Tryptophan; p is an integer with a minimum value of 2.

2. (currently amended) A vaccine as defined in claim 1 wherein the peptide is a linear or cyclic peptide[s] comprising units of formula[:]  
selected from the group consisting of:

(a)  $(A)_n$  wherein A is Lysine or Arginine and n is an integer with a value of 7 to 16; (b)  $(AB)_m$  wherein A is Lysine or Arginine and B is a hydrophobic amino acid selected from the group consisting of Valine, Leucine, Isoleucine, Tyrosine, Phenylalanine and Tryptophan; m is an integer with a value of 4 to 20; and (c)  $(ABC)_p$  wherein A is a cationic amino acid which is Lysine or Arginine; B and C are hydrophobic amino acids which may be the same or different and are selected from the group consisting of Valine, Leucine, Isoleucine, Tyrosine, Phenylalanine and Tryptophan; p is an integer with a value of 4 to 20.

3. (previously presented) A vaccine as defined in claim 1 wherein the LPS is derived from N. meningitidis.

4. (previously presented) A vaccine as defined in claim 1 wherein the LPS is derived from Salmonella typhi.

5. (previously presented) A vaccine as defined in claim 1 where the amount of peptide is from 2-10 to 2-5000 times the weight of the LPS.

6. (previously presented) A vaccine as defined in claim 1 wherein the peptide has units comprising  $(AB)_m$ .

7. (previously presented) A vaccine as defined in claim 1 wherein the peptide has units comprising  $(ABC)_p$ .
8. (previously presented) A vaccine as defined in claim 1 wherein the peptide comprises:  $(Lys)_{10}$  (SEQ ID NO: 1).
9. (canceled).
10. (previously presented) A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide, on a weight basis relative to said LPS wherein the peptide comprises:  $(Lys-Phe)_5$  (SEQ ID NO: 5).
11. (previously presented) A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises: Lys-Phe-Leu-Lys-Lys-Thr-Leu (SEQ ID NO: 6).
12. (previously presented) A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises:  $(Lys-Phe-Leu)_2-Lys$  (SEQ ID NO: 7).
13. previously presented) A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form

with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises: (Lys-Phe-Leu)<sub>3</sub>-Lys (SEQ ID NO: 8).

14. (previously presented) A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises: (Arg-Tyr-Val)<sub>3</sub> (SEQ ID NO: 9).

15. (previously presented) A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises: (Lys-Phe-Phe)<sub>3</sub>-Lys (SEQ ID NO: 10).

16. (previously presented) A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises: (Lys-Leu-Leu)<sub>3</sub> (SEQ ID NO: 11).

17. (previously presented) A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises: (Lys)<sub>6</sub> (Phe-Lys)<sub>2</sub> (SEQ ID NO: 12).

18. (canceled).

19. (previously presented) A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises:

Cys-Lys-Phe-Lys-Lys-Cys

s-----s (SEQ ID NO: 14).

20. (previously presented) A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises:

Lys-Phe-Lys-Cys-Lys-Phe-Lys-Phe-Lys-Cys

s-----s (SEQ ID NO: 15).

21. (previously presented) A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises:

Lys-Leu-Lys-Cys-Lys-Leu-Lys-Leu-Lys-Cys

s-----s (SEQ ID NO: 16).

22. (previously presented) A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises:

Arg-Thr-Arg-Cys-Arg-Phe-Lys-Arg-Arg-Cys

s-----s (SEQ ID NO: 17).

23. (previously presented) A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises:

Lys-Cys-(Lys-Phe-Lys)<sub>2</sub>-Cys-Lys

s-----s (SEQ ID NO: 18).

24. (previously presented) A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises:

Cys-(Lys)<sub>4</sub>-(Phe)<sub>4</sub>-Cys

s-----s (SEQ ID NO: 19).

25. (previously presented) A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises:

Cys-(Lys-Phe-Leu)<sub>3</sub>-Lys-Cys

s-----s (SEQ ID NO: 20).

26. (previously presented) A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises:

Val-Lys-Ala-Leu-Arg-Val-Arg-Arg-Leu (SEQ ID NO: 21).

27. (previously presented) A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises:

Lys-Ser-Leu-Ser-Leu-Lys-Arg-Leu-Thr-Tyr-Arg (SEQ ID NO: 22).

28. (previously presented) A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises:

Lys-Val-Arg-Lys-Ser-Phe-Phe-Lys-Val (SEQ ID NO: 23).

29. (previously presented) A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises:

Phe-Leu-Lys-Pro-Gly-Lys-Val-Lys-Val (SEQ ID NO: 24).



30. (previously presented) A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide is of the formula:

Lys-Glu-Leu-Lys-Arg-Ile-Lys-Ile (SEQ ID NO: 25).

31. (previously presented) A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide is of the formula:

Lys-Trp-Lys-Ala-Gln-Lys-Arg-Phe-Leu (SEQ ID NO: 26).

32. (previously presented) A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide is of the formula:

Lys-Trp-Lys-Ala-Gln-Lys-Arg-Phe-Leu-Lys (SEQ ID NO: 27).

33. (previously presented) A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide is of the formula:

Lys-Arg-Leu-Lys-Trp-Lys-Tyr-Lys-Gly-Lys-Phe (SEQ ID NO: 28).

34. (previously presented) A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide is of the formula:

Lys-Thr-Lys-Cys-Lys-Phe-Leu-Lys-Lys-Cys

s-----s (SEQ ID NO: 31).

35. (previously presented) A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide is of the formula:

Cys-Lys-Phe-Leu-Lys-Lys-Cys

s-----s (SEQ ID NO: 30).

36. (canceled).

37. (previously presented) A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide is of the formula:

Lys-Phe-Leu-Lys-Lys-Thr (SEQ ID NO: 32).

38. (previously presented) A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form

with a stoichiometric excess of a peptide on a weight basis relative to said LPS  
wherein the peptide is of the formula:

Cys-Lys-Lys-Leu-Phe-Lys-Cys-Lys-Thr-Lys  
s-----s (SEQ ID NO: 33).

39. (previously presented) A vaccine for preventing gram-negative infections  
which comprises a complex obtained by combining LPS free or in conjugate form  
with a stoichiometric excess of a peptide on a weight basis relative to said LPS  
wherein the peptide is of the formula:

Cys-Lys-Lys-Leu-Phe-Lys-Cys-Lys-Thr  
s-----s (SEQ ID NO: 34).

40. (previously presented) A vaccine for preventing gram-negative infections  
which comprises a complex obtained by combining LPS free or in conjugate form  
with a stoichiometric excess of a peptide on a weight basis relative to said LPS  
wherein the peptide is of the formula:

Ile-Lys-Thr-Lys-Cys-Lys-Phe-Leu-Lys-Lys-Cys  
s-----s (SEQ ID NO: 35).

41. (previously presented) A vaccine for preventing gram-negative infections  
which comprises a complex obtained by combining LPS free or in conjugate form  
with a stoichiometric excess of a peptide on a weight basis relative to said LPS  
wherein the peptide is of the formula:

Ile-Lys-Thr-Lys-Lys-Phe-Leu-Lys-Lys-Thr (SEQ ID NO: 36).

42. (previously presented) A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises:

Ile-Lys-Phe-Leu-Lys-Phe-Leu-Lys-Phe-Leu-Lys (SEQ ID NO: 37).

43. (previously presented) A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises:

Lys-Phe-Leu-Lys-Phe-Leu-Lys (SEQ ID NO: 38).

44. (previously presented) A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises:

Arg-Tyr-Val-Arg-Tyr-Val-Arg-Tyr-Val (SEQ ID NO: 39).

45. (previously presented) A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises:

Lys-Phe-Phe-Lys-Phe-Phe-Lys-Phe-Cys (SEQ ID NO: 40).

46. (previously presented) A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises:

Ile-Lys-Phe-Leu-Lys-Phe-Leu-Lys-Phe-Leu (SEQ ID NO: 41).

47. (previously presented) A vaccine for preventing gram-negative infections which comprises complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide is of the formula:

(Lys)<sub>6</sub>Phe-Leu-Phe-Leu (SEQ ID NO: 42).

48. (previously presented) A vaccine as defined in claim 1 wherein the peptide comprises:

Cys-Lys-Phe-Lys-Phe-Lys-Phe-Lys-Phe-Cys

s-----s (SEQ ID NO : 43).

49. (previously presented) A vaccine for preventing gram-negative infections which comprises complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of peptide on a weight basis relative to said LPS wherein the peptide is of the formula:

Lys-Trp-Lys-Ala-Gln-Lys-Arg-Phe-Leu-Lys (SEQ ID NO: 44).

50. (previously presented) A vaccine as defined in claim 1 wherein the peptide comprises:

Lys-Arg-Leu-Lys-Trp-Lys-Tyr-Lys-Gly-Lys-Phe (SEQ ID NO: 45).

51. (currently amended) A method for the preparation of a vaccine for prevention of gram-negative infections, said method comprising combining LPS with a stoichiometric excess of a peptide on a weight basis relative to said LPS, said peptide [comprising:] selected from the group consisting of:
- (a)  $(A)_n$  wherein A is Lysine or Arginine and n is an integer with a minimum value of 7; (b)  $(AB)_m$  wherein A is Lysine or Arginine and B is a hydrophobic amino acid selected from the group consisting of Valine, Leucine, Isoleucine, Tyrosine, Phenylalanine and Tryptophan; m is an integer with a minimum value of 3; and (c)  $(ABC)_p$  wherein A is a cationic amino acid which is Lysine or Arginine; B and C are hydrophobic amino acids which may be the same or different and are selected from the group consisting of Valine, Leucine, Isoleucine, Tyrosine, Phenylalanine and Tryptophan; p is an integer with a minimum value of 2.
52. (previously presented) A vaccine as defined in claim 1 which is combined or administered with other vaccine components.
53. (previously presented) A vaccine as defined in claim 1 which contains an LPS peptide complex derived from more than one species of bacteria.
54. (currently amended) A vaccine for prevention of gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide:LPS where there is an

excess of from 2 to 5000 times by weight of peptide, said peptide [comprising:]  
being selected from the group consisting of:

(a)  $(A)_n$  wherein A is Lysine or Arginine and n is an integer with a minimum value of 7; (b)  $(AB)_m$  wherein A is Lysine or Arginine and B is a hydrophobic amino acid selected from the group consisting of Valine, Leucine, Isoleucine, Tyrosine, Phenylalanine and Tryptophan; m is an integer with a minimum value of 3; and (c)  $(ABC)_p$  wherein A is a cationic amino acid which is Lysine or Arginine; B and C are hydrophobic amino acids which may be the same or different and are selected from the group consisting of Valine, Leucine, Isoleucine, Tyrosine, Phenylalanine and Tryptophan; p is an integer with a minimum value of 2.

55. (previously presented) A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS in a free form or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS of the formula:

Cys-(Lys)<sub>5</sub>-Cys

s-----s ( SEQ ID NO: 13).

56. (previously presented) A vaccine as defined in claim 1 wherein the LPS is derived from non-typable H. influenzae.

57. (previously presented) A vaccine as defined in claim 1 wherein the LPS is derived from N. meningitidis, H. influenzae, Moraxella catharralis, Pseudomonas aeruginosa, Salmonella enterica and Escherichia coli.

58. (previously presented) A vaccine as defined in claim 57 wherein the LPS is derived from Salmonella enterica.

59. (previously presented) A vaccine as defined in claim 57 wherein the LPS is derived from H. influenzae.

60. (previously presented) A vaccine as defined in claim 57 wherein the LPS is derived from N. meningitidis.

61. (previously presented) A vaccine as defined in claim 57 wherein the LPS is derived from Moraxella catharralis.

62. (previously presented) A vaccine as defined in claim 57 wherein the LPS is derived from Escherichia coli.

63. (currently amended) A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of peptide:LPS where there is an excess of from 2 to 2500 times by weight of peptide, said peptide consisting essentially of a peptide selected from the group consisting of:

(a)  $(A)_n$  wherein A is Lysine or Arginine and n is an integer with a minimum value of 7; (b)  $(AB)_m$  wherein A is Lysine or Arginine and B is a hydrophobic amino acid selected from the group consisting of Valine, Leucine, Isoleucine, Tyrosine, Phenylalanine and Tryptophan; m is an integer with a minimum value of 3; and (c)  $(ABC)_p$  wherein A is a cationic amino acid which is Lysine or Arginine; B and C



are hydrophobic amino acids which may be the same or different and are selected from the group consisting of Valine, Leucine, Isoleucine, Tyrosine, Phenylalanine and Tryptophan; p is an integer with a minimum value of 2.

64. (previously presented) A vaccine for preventing gram-negative infections as defined in claim 63 which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of peptide:LPS where there is an excess of from 250 to 2500 times by weight of peptide.

Claims 1-8, 10-17, 19-35 and 37-64 have been allowed and renumbered 1-61 respectively.

It is noted that the formal drawings are now required and that Applicant should comply with the objections to the drawings as set forth in Form 948 (Draftsperson's Notice) mailed with Paper No. 5 (October 5, 1999). Applicant should make sure that the figure descriptions set forth in the specification match the formal drawings that will be submitted.

The following is an examiner's statement of reasons for allowance: the closest prior art of Porro (WO 95/03327) does not disclose or teach using a stoichiometric excess of peptide relative to the LPS; Porro teaches a one to one ratio of the peptide to LPS.

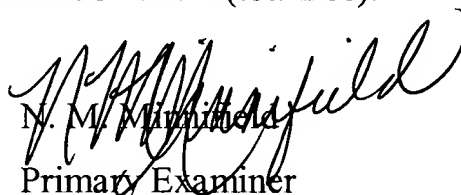
Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should

preferably accompany the issue fee. Such submissions should be clearly labeled  
“Comments on Statement of Reasons for Allowance.”

Any inquiry concerning this communication or earlier communications from the examiner should be directed to N. M. Minnifield whose telephone number is 571-272-0860. The examiner can normally be reached on M-F (8:00-5:30) Second Friday Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette R.F. Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
N. M. Minnifield  
Primary Examiner

Art Unit 1645

NMM

April 3, 2005

## ***CLEAN COPY OF CLAIMS***

1. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide, on a weight basis relative to said LPS, said peptide selected from the group consisting of:

(a)  $(A)_n$  wherein A is Lysine or Arginine and n is an integer with a minimum value of 7; (b)  $(AB)_m$  wherein A is Lysine or Arginine and B is a hydrophobic amino acid selected from the group consisting of Valine, Leucine, Isoleucine, Tyrosine, Phenylalanine and Tryptophan; m is an integer with a minimum value of 3; and (c)  $(ABC)_p$  wherein A is a cationic amino acid which is Lysine or Arginine; B and C are hydrophobic amino acids which may be the same or different and are selected from the group consisting of Valine, Leucine, Isoleucine, Tyrosine, Phenylalanine and Tryptophan; p is an integer with a minimum value of 2.

2. A vaccine as defined in claim 1 wherein the peptide is a linear or cyclic peptide comprising units of formula selected from the group consisting of:

(a)  $(A)_n$  wherein A is Lysine or Arginine and n is an integer with a value of 7 to 16; (b)  $(AB)_m$  wherein A is Lysine or Arginine and B is a hydrophobic amino acid selected from the group consisting of Valine, Leucine, Isoleucine, Tyrosine, Phenylalanine and Tryptophan; m is an integer with a value of 4 to 20; and (c)  $(ABC)_p$  wherein A is a cationic amino acid which is Lysine or Arginine; B and C are hydrophobic amino acids which may be the same or different and are selected from the group consisting of Valine, Leucine, Isoleucine, Tyrosine, Phenylalanine and Tryptophan; p is an integer with a value of 4 to 20.

3. A vaccine as defined in claim 1 wherein the LPS is derived from N. meningitidis.
4. A vaccine as defined in claim 1 wherein the LPS is derived from Salmonella typhi.
5. A vaccine as defined in claim 1 where the amount of peptide is from 2-10 to 2-5000 times the weight of the LPS.
6. A vaccine as defined in claim 1 wherein the peptide has units comprising  $(AB)_m$ .
7. A vaccine as defined in claim 1 wherein the peptide has units comprising  $(ABC)_p$ .
8. A vaccine as defined in claim 1 wherein the peptide comprises:  $(Lys)_{10}$  (SEQ ID NO: 1).
10. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide, on a weight basis relative to said LPS wherein the peptide comprises:  $(Lys-Phe)_5$  (SEQ ID NO: 5).
11. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a

stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises: Lys-Phe-Leu-Lys-Lys-Thr-Leu (SEQ ID NO: 6).

12. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises: (Lys-Phe-Leu)<sub>2</sub>-Lys (SEQ ID NO: 7).

13. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises: (Lys-Phe-Leu)<sub>3</sub>-Lys (SEQ ID NO: 8).

14. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises: (Arg-Tyr-Val)<sub>3</sub> (SEQ ID NO: 9).

15. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises: (Lys-Phe-Phe)<sub>3</sub>-Lys (SEQ ID NO: 10).

16. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a

stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises: (Lys-Leu-Leu)<sub>3</sub> (SEQ ID NO: 11).

17. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises: (Lys)<sub>6</sub> (Phe-Lys)<sub>2</sub> (SEQ ID NO: 12).

19. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises:

Cys-Lys-Phe-Lys-Lys-Cys

s-----s (SEQ ID NO: 14).

20. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises:

Lys-Phe-Lys-Cys-Lys-Phe-Lys-Phe-Lys-Cys

s-----s (SEQ ID NO: 15).

21. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a

stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises:

Lys-Leu-Lys-Cys-Lys-Leu-Lys-Leu-Lys-Cys

s-----s (SEQ ID NO: 16).

22. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises:

Arg-Thr-Arg-Cys-Arg-Phe-Lys-Arg-Arg-Cys

s-----s (SEQ ID NO: 17).

23. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises:

Lys-Cys-(Lys-Phe-Lys)<sub>2</sub>-Cys-Lys

s-----s (SEQ ID NO: 18).

24. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises:

Cys-(Lys)<sub>4</sub>-(Phe)<sub>4</sub>-Cys

s-----s (SEQ ID NO: 19).

25. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises:

Cys-(Lys-Phe-Leu)<sub>3</sub>-Lys-Cys  
s-----s (SEQ ID NO: 20).

26. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises:

Val-Lys-Ala-Leu-Arg-Val-Arg-Arg-Leu (SEQ ID NO: 21).

27. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises:

Lys-Ser-Leu-Ser-Leu-Lys-Arg-Leu-Thr-Tyr-Arg (SEQ ID NO: 22).

28. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises:

Lys-Val-Arg-Lys-Ser-Phe-Phe-Lys-Val (SEQ ID NO: 23).



29. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises:

Phe-Leu-Lys-Pro-Gly-Lys-Val-Lys-Val (SEQ ID NO: 24).

30. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide is of the formula:

Lys-Glu-Leu-Lys-Arg-Ile-Lys-Ile (SEQ ID NO: 25).

31. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide is of the formula:

Lys-Trp-Lys-Ala-Gln-Lys-Arg-Phe-Leu (SEQ ID NO: 26).

32. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide is of the formula:

Lys-Trp-Lys-Ala-Gln-Lys-Arg-Phe-Leu-Lys (SEQ ID NO: 27).

33. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide is of the formula:

Lys-Arg-Leu-Lys-Trp-Lys-Tyr-Lys-Gly-Lys-Phe (SEQ ID NO: 28).

34. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide is of the formula:

Lys-Thr-Lys-Cys-Lys-Phe-Leu-Lys-Lys-Cys

s-----s (SEQ ID NO: 31).

35. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide is of the formula:

Cys-Lys-Phe-Leu-Lys-Lys-Cys

s-----s (SEQ ID NO: 30).

37. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide is of the formula:

Lys-Phe-Leu-Lys-Lys-Thr (SEQ ID NO: 32).

38. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide is of the formula:

Cys-Lys-Lys-Leu-Phe-Lys-Cys-Lys-Thr-Lys  
s-----s (SEQ ID NO: 33).

39. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide is of the formula:

Cys-Lys-Lys-Leu-Phe-Lys-Cys-Lys-Thr  
s-----s (SEQ ID NO: 34).

40. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide is of the formula:

Ile-Lys-Thr-Lys-Cys-Lys-Phe-Leu-Lys-Lys-Cys  
s-----s (SEQ ID NO: 35).

41. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a

stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide is of the formula:

Ile-Lys-Thr-Lys-Lys-Phe-Leu-Lys-Lys-Thr (SEQ ID NO: 36).

42. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises:

Ile-Lys-Phe-Leu-Lys-Phe-Leu-Lys-Phe-Leu-Lys (SEQ ID NO: 37).

43. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises:

Lys-Phe-Leu-Lys-Phe-Leu-Lys (SEQ ID NO: 38).

44. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises:

Arg-Tyr-Val-Arg-Tyr-Val-Arg-Tyr-Val (SEQ ID NO: 39).

45. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a

stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises:

Lys-Phe-Phe-Lys-Phe-Phe-Lys-Phe-Cys (SEQ ID NO: 40).

46. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide comprises:

Ile-Lys-Phe-Leu-Lys-Phe-Leu-Lys-Phe-Leu (SEQ ID NO: 41).

47. A vaccine for preventing gram-negative infections which comprises complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS wherein the peptide is of the formula:

(Lys)<sub>6</sub>Phe-Leu-Phe-Leu (SEQ ID NO: 42).

48. A vaccine as defined in claim 1 wherein the peptide comprises:

Cys-Lys-Phe-Lys-Phe-Lys-Phe-Lys-Phe-Cys

s-----s (SEQ ID NO : 43).

49. A vaccine for preventing gram-negative infections which comprises complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of peptide on a weight basis relative to said LPS wherein the peptide is of the formula:

Lys-Trp-Lys-Ala-Gln-Lys-Arg-Phe-Leu-Lys (SEQ ID NO: 44).

50. A vaccine as defined in claim 1 wherein the peptide comprises:

Lys-Arg-Leu-Lys-Trp-Lys-Tyr-Lys-Gly-Lys-Phe (SEQ ID NO: 45).

51. A method for the preparation of a vaccine for prevention of gram-negative infections, said method comprising combining LPS with a stoichiometric excess of a peptide on a weight basis relative to said LPS, said peptide selected from the group consisting of:

(a)  $(A)_n$  wherein A is Lysine or Arginine and n is an integer with a minimum value of 7; (b)  $(AB)_m$  wherein A is Lysine or Arginine and B is a hydrophobic amino acid selected from the group consisting of Valine, Leucine, Isoleucine, Tyrosine, Phenylalanine and Tryptophan; m is an integer with a minimum value of 3; and (c)  $(ABC)_p$  wherein A is a cationic amino acid which is Lysine or Arginine; B and C are hydrophobic amino acids which may be the same or different and are selected from the group consisting of Valine, Leucine, Isoleucine, Tyrosine, Phenylalanine and Tryptophan; p is an integer with a minimum value of 2.

52. A vaccine as defined in claim 1 which is combined or administered with other vaccine components.

53. A vaccine as defined in claim 1 which contains an LPS peptide complex derived from more than one species of bacteria.

54. A vaccine for prevention of gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a

stoichiometric excess of a peptide:LPS where there is an excess of from 2 to 5000 times by weight of peptide, said peptide being selected from the group consisting of:

(a)  $(A)_n$  wherein A is Lysine or Arginine and n is an integer with a minimum value of 7; (b)  $(AB)_m$  wherein A is Lysine or Arginine and B is a hydrophobic amino acid selected from the group consisting of Valine, Leucine, Isoleucine, Tyrosine, Phenylalanine and Tryptophan; m is an integer with a minimum value of 3; and (c)  $(ABC)_p$  wherein A is a cationic amino acid which is Lysine or Arginine; B and C are hydrophobic amino acids which may be the same or different and are selected from the group consisting of Valine, Leucine, Isoleucine, Tyrosine, Phenylalanine and Tryptophan; p is an integer with a minimum value of 2.

55. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS in a free form or in conjugate form with a stoichiometric excess of a peptide on a weight basis relative to said LPS of the formula:

Cys-(Lys)<sub>5</sub>-Cys

s-----s ( SEQ ID NO: 13).

56. A vaccine as defined in claim 1 wherein the LPS is derived from non-typable H. influenzae.

57. A vaccine as defined in claim 1 wherein the LPS is derived from N. meningitidis, H. influenzae, Moraxella catharralis, Pseudomonas aeruginosa, Salmonella enterica and Escherichia coli.

58. A vaccine as defined in claim 57 wherein the LPS is derived from Salmonella enterica.
59. A vaccine as defined in claim 57 wherein the LPS is derived from H. influenzae.
60. A vaccine as defined in claim 57 wherein the LPS is derived from N. meningitidis.
61. A vaccine as defined in claim 57 wherein the LPS is derived from Moraxella catharralis.
62. A vaccine as defined in claim 57 wherein the LPS is derived from Escherichia coli.
63. A vaccine for preventing gram-negative infections which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of peptide:LPS where there is an excess of from 2 to 2500 times by weight of peptide, said peptide consisting essentially of a peptide selected from the group consisting of:
- (a)  $(A)_n$  wherein A is Lysine or Arginine and n is an integer with a minimum value of 7; (b)  $(AB)_m$  wherein A is Lysine or Arginine and B is a hydrophobic amino acid selected from the group consisting of Valine, Leucine, Isoleucine, Tyrosine, Phenylalanine and Tryptophan; m is an integer with a minimum value of 3; and (c)



$(ABC)_p$  wherein A is a cationic amino acid which is Lysine or Arginine; B and C are hydrophobic amino acids which may be the same or different and are selected from the group consisting of Valine, Leucine, Isoleucine, Tyrosine, Phenylalanine and Tryptophan; p is an integer with a minimum value of 2.

64. A vaccine for preventing gram-negative infections as defined in claim 63 which comprises a complex obtained by combining LPS free or in conjugate form with a stoichiometric excess of peptide:LPS where there is an excess of from 250 to 2500 times by weight of peptide.